

Notice of Allowability

Application No.

09/830,986

Applicant(s)

BERNKOP-SCHNURCH,
ANDREAS

Examiner

Umamaheswari Ramachandran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 8/29/2007.
2. ☒ The allowed claim(s) is/are 1,28,29,31-33,35-38,56-66,92-97 and 110-117.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

DETAILED ACTION***Status of Claims***

The examiner notes the receipt of the amendments and remarks received in the office on 8/29/2007 amending claims 1, 28, 29, 31-33, 35-38, 56-66, 92-97 and 110 and canceling claims 39-55, 67-73, 75-91, and 98-109 and adding new claims 111-117 have been added. Claims 2-27, 30, 34, 39-55, 67-91, 98-109 are cancelled.

Application Priority

This application is a 371 of PCT/ AT99/00265 11/04/1999 and claims priority of the foreign application Austria A 1828/98, 11/04/1998. The specification of the priority document (certified copy of the foreign priority document, Australian Application No. 1828/98) does not provide support of the said thiolated polymers of claim 1: thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers. Hence the applicant is granted priority only to Nov 4 1999 as the filing date for the application.

REASONS FOR ALLOWANCE

Claims 1, 28, 29, 31-33, 35-38, 110 rejected under 35 U.S.C. 112, first paragraph is withdrawn due to the amendment of claim 1. Claims 1, 28, 29, 31-33, 35-38, 110 rejected under 35 U.S.C. 112, second paragraph is withdrawn due to the amendment of claim 1. The closest prior art of record are 1) by Bernkop-Schnurch et al (Pharmaceutical Research, Vol. 16, No. 6, 1999). 2) Omura et al (U.S. 5,064,495 3)

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Constancis et al (U.S. 5,646,239) 3) Marchant US Patent 6,514,535). Claims 1, 28, 29, 31-33, 35-38, 56-66, 92-97 and 111-117 are allowable and are renumbered.

The claims of the instant invention are directed to 1) thiolated mucoadhesive polymer selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid. and thiolated polymer of pectin wherein (a) said thiolated mucoadhesive polymer comprises at least one non-terminal thiol group, and (b) said thiolated mucoadhesive polymer exhibits a total work of adhesion (TWA) of more than 120 μ J to intestinal mucosa at a pH of 7 2) A method of preparing a thiolated mucoadhesive polymers, said method comprising: providing base polymers comprising at least one non-terminal monomer that includes a terminal, functional group I, wherein said terminal functional group I is free within said polymer, providing thiol-containing compounds, wherein said thiol-containing compounds include at least one further functional group II, and wherein said functional groups I and II are together capable of forming a covalent bond, and reacting said base polymers with said thiol-containing groups, wherein said terminal functional group 1 forms a covalent bond with said functional group II to produce a thiolated mucoadhesive polymer of claim 1.

Bernkop-Schnurch et al teaches the improvement of mucoadhesive properties of polymer polycarbophil (copolymer of acrylic acid and divinyl glycol) by thiolating them with sulfhydryl groups. The reference further teaches the values of TWA of polymer-

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cysteine conjugate 16:1 to be $191 \pm 47 \mu\text{J}$ and $280 \pm 67 \mu\text{J}$ for the polymer-cysteine conjugate 2:1 at pH 6.8. The reference teaches that cysteine is covalently bound to the polymer by the formation of amide bonds. The reference teaches that the polymer has at least one free thiol group as demonstrated by the mucin binding studies. However, the prior art rejection has been overcome due to the declaration (submitted 3/13/2007) by the inventor that he is the sole author of the reference and the co-authors did not have any role in inventing the subject matter.

Omura discloses methods of improving adhesion properties of a polymer to a metallic compound wherein the polymeric compositions contains at least one mercapto or thiol group that is not a non-terminal thiol group. Omura describes that the polymeric entity is prepared by condensation of methacrylic acid or anhydrides that contain a non-terminal thiol (mercapto unit). The reference do not teach the thiolated polymers of the instant invention namely, thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid. and thiolated polymer of pectin. Therefore, there is no anticipation or motivation of making thiolated polymers of the instant invention from the teaching or suggestion from prior art.

Constancis teaches oligomeric moieties that contain a side chain thiol group at position R1 or R2. Constancis teaches that the copolymer is a function of the combination of succinic acid and cysteine. Constancis further states that his oligomers can be attached to biological macromolecules such as mucopolysaccharides including

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hyaluronic acid, chitosan and cellulose to render such polymers thiolated. However, Constancis does not disclose thiolated polymers. The declaration by Dr. Bernkop-Shnurch (Submitted Aug 7 2003, also submitted as Exhibit A) showed that the Constancis polymers were not mucoadhesive and did not exhibit a TWA of at least 120 μ J. Therefore, there is no anticipation or motivation of making of making thiolated polymers of the instant invention from the teaching or suggestion from prior art.

Merchant describes bioadhesive compositions comprising mucoadhesive polymeric units containing at least one non-terminal thiol group on the side chains and the monomeric unit can contain cysteine. Merchant specifically states that his compositions contain an active agent attached to a polymer with thiol side group which can be used to delivery the active thiol containing therapeutic formulations. However, the reference do not teach the thiolated polymers of the instant invention namely, thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid. and thiolated polymer of pectin. Therefore, there is no anticipation or motivation of making thiolated polymers of the instant invention from the teaching or suggestion from prior art.

The claims directed to mucoadhesive thiolated polymers are free of prior art. Hence the method of making the mucoadhesive thiolated polymer claims is allowable.

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The claims are allowable over the closest art of record because they do not teach, disclose nor make obvious the claimed mucoadhesive thiolated polymers and the method of making the claimed mucoadhesive thiolated polymers.

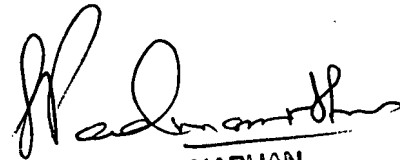
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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